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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/975,812 | 10/11/2001 | Gavril Pasternak | 830010-2002.2 | 9302 |

20999 7590 02/26/2003

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| EXAMINER |
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WANG, SHENGJUN

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| ART UNIT | PAPER NUMBER |
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1617

DATE MAILED: 02/26/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/975,812

Applicant(s)

PASTERNAK ET AL.

Examiner

Shengjun Wang

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11,16-20 and 22-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11,16-20 and 22-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9,13.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

The Request for a Continued Examination (RCE) under 37 CFR 1.114 filed on December 2, 2002 based on parent Application No. 09/975812 is acceptable and a RCE has been established. An action on the RCE follows.

Claim Rejections 35 U.S.C. 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 11, 16-20, and 22-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The particular limitation in claim 11, "to potentiate a synergistic antinociceptive response at peripheral at peripheral sites" lack support from the specification or claims as original filed.

Claim Rejections 35 U.S.C. § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 11, 16-20, and 22-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stein (US 5, 948,389, of record) in view of Saito (IDS, AF).

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3. Stein teaches a method of enhancing analgesic effects of locally applied opioid analgesic or anesthetic agent, see particularly, the abstract, claims 1, and column 3, line 25 bridging column 4, line 11. Stein also teaches morphine as opioid analgesic and lidocaine as a local anesthetic agent, see, particularly, claims 3 and 5. Stein also teaches that the active ingredients in its compositions are present in an amount of 0.5% to 95% by weight of the composition, see, particularly, col. 7, lines 52-55. Finally Stein teaches that its composition can be applied topically in various known topical formulation. See, particularly, col. 7, lines 56-59.

4. Stein does not teach expressly the employment of a combination of morphine and lidocaine in a topical composition, or the particular amounts of each and every ingredient in the composition.

5. However, Saito et al. teach that employment of combination of lidocaine and morphine are well known in the art. See, particularly, page 1455. Saito et al. further establish that co-administering of morphine and lidocaine provides synergistic antinociceptive effects. See, particularly, page 1455. Saito's results support a well-known hypothesis that such combination would produce synergy and cause reduction of dose, resulting in a low incidence of adverse side effect associated with each drug. See, particularly, page 1461, the last three paragraphs.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to make and use a topical composition which comprises morphine and lidocaine.

A person of ordinary skill in the art would have been motivated to make and use a topical composition, which comprises morphine and lidocaine because lidocaine and morphine in combination are known to provide synergistic antinociceptive effects, and because they are

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known to be employed in combination. Further, intraconversion of dosage forms and optimization of the effective amounts of each ingredient to provide a known synergistic effect are within the skill of artisan and are therefore obvious. Regarding the particular limitation about the sites of synergistic antinociceptive response, note since the references teach synergistic antinociceptive effects generally, and would encompass any synergistic antinociceptive response.

Response to the Arguments

Applicants' amendments and remarks submitted December 2, 2002 have been fully considered, but are not persuasive for reasons discussed below.

6. The declaration filed on December 2, 2002 under 37 CFR 1.131 has been considered but is ineffective because the exhibit A mentioned in the declaration has not been received.

Applicants' remarks regarding the state of the art about topical application of opioid analgesia, and/or lidocaine, and the cited references therein are not probative in view of Stein's teaching. Stein expressly teaches topical application of opioid analgesia. See the rejection above.

7. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Particularly, Stain teaches method of topical application of opioid analgesia and/or local anesthetic agents with enhanced effects. Saito teaches that employment of the combination is well-known in the art and are known to provide synergistic effect, consider the cited references as a whole, the claimed method would have been obvious.

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Applicants argue that the cited references fails to result in the claimed use, citing Saito et al. teach systemic administration. First, Saito et al do not limit the teaching to systemic administration only. In fact, Saito suggest generally the synergistic effect of the combination of opioid analgesia and local anesthetic agent. (See the last three paragraphs at page 1461). Further, Stain expressly teaches enhanced effect of topical application of opioid analgesia and local anesthetic agent, contrary to the references cited by applicants.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang, Ph.D. whose telephone number is (703) 308-4554. The examiner can normally be reached on Monday-Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Examiner



Shengjun Wang

February 20, 2003


RUSSELL TRAVERS
PRIMARY EXAMINER
GROUP 1200